1.3.1.1 PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE

SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

BETANOID TABLETS 0,5 mg tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet of BETANOID TABLETS contains 0,5 mg of betamethasone.

Sugar free

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablets

BETANOID TABLETS is a white, flat bevelled edged tablet with a breakline on the one side and plain on the other side.

The score line is only to facilitate breaking for ease of swallowing and not to divide into equal doses**.**

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

BETANOID TABLETS is indicated for symptomatic treatment of inflammatory conditions where a steroid is indicated.

4.2. Posology and method of administration

Posology

Dosing requirements are variable and must be individualised on the basis of the specific disease, its severity and the response of the patient.

Betamethasone has a usual dose range of 0,5 mg to 5 mg daily in divided doses (1 to 10 BETANOID TABLETS) depending on the specific disease being treated.

In situations of less severity, low doses generally will suffice while in selected patients higher initial doses may be required.

The initial dose should be maintained or adjusted until a satisfactory response is observed.

If a period of spontaneous remission occurs in a chronic condition, treatment should be discontinued.

Once a day dosage:
The total daily maintenance dose can be administered once early in the morning.

Paediatric population

Dosages for infants and children should be governed by the same considerations as adults rather than strict adherence to ratios indicated by age or body weight.

Method of administration

For oral administration.

4.3 Contraindications

BETANOID TABLETS is contraindicated in:

- Patients with hypersensitivity to betamethasone or to any excipients in BETANOID TABLETS (see section 6.1).
- Patients with hypersensitivity to corticosteroids.
- Patients with systemic fungal infections.
- Patients with peptic ulceration, osteoporosis, psychosis or severe psychoneurosis.
- Patients with active or doubtfully quiescent tuberculosis should not be given corticosteroids except, very rarely, as adjuncts to treatment with anti-tubercular medicine.
- In the presence of acute viral infections including herpes zoster or herpes simplex ulceration of the eye.
- Vaccination with live vaccines.

The safety and use of BETANOID TABLETS during pregnancy and in lactation has not been established.

4.4 Special warnings and precautions for use

Undesirable effects may be minimised by using the lowest effective dose for the minimum period and by administering the daily requirement as a single morning dose, or whenever possible as a single morning dose on alternate days.

Frequent patient review is required to appropriately titrate the dose against disease activity.

Myocardial infarction

Caution is advised with the use of corticosteroids, as in BETANOID TABLETS in patients who have suffered a recent myocardial infarction because of the risk of myocardial rupture.

Hypothyroidism and myasthenia gravis

Caution is advised on the use of corticosteroids, as in BETANOID TABLETS in patients with hypothyroidism or myasthenia gravis.

Suppression of the inflammatory response and immune function

BETANOID TABLETS may mask some signs of infection.

Suppression of the inflammatory response and immune function increases the susceptibility to all kinds of infection, including sepsis and fungal infections and their severity. The clinical presentation may often be atypical and serious infections such as septicaemia and tuberculosis may be masked and may reach an advanced stage before being recognised.

Infectious diseases

Chickenpox is of particular concern since this normally minor illness may be fatal in immunosuppressed patients. Patients (or parents of children) without a definite history of chickenpox should be advised to avoid close personal contact with chickenpox or herpes zoster and if exposed they should seek urgent medical attention. Passive immunisation with varicella zoster immunoglobulin (VZIG) is needed by exposed non-immune patients who are receiving systemic corticosteroids or who have used them within the previous months; this should be given within 10 days of exposure to chickenpox. If a diagnosis of chickenpox is confirmed, the illness warrants specialist care and urgent treatment.

Corticosteroids should, such as BETANOID TABLETS not be stopped and the dose may need to be increased.

Patients should be advised to take particular care to avoid exposure to measles and to seek immediate medical advice if exposure occurs. Prophylaxis with intramuscular normal immunoglobulin may be needed.

Vaccines

Live vaccines should not be given to individuals with impaired immune responsiveness. The antibody response to other vaccines may be diminished.

Adrenal suppression

Adrenal cortical atrophy develops during prolonged therapy and may persist for years after stopping treatment.

In patients who have received more than physiological doses of systemic corticosteroids (approximately 1 mg betamethasone or equivalent) for greater than 3 weeks, withdrawal should not be abrupt. How dose reduction should be carried out depends largely on whether the disease is likely to relapse as a dose of systemic corticosteroids is reduced. Clinical assessment of disease activity may be needed during withdrawal. If the disease is unlikely to relapse on withdrawal of systemic corticosteroids but there is uncertainty about hypothalamic-pituitary-adrenal (HPA) suppression, the dose of systemic corticosteroid may be reduced rapidly to physiological doses. Once a daily dose equivalent to 1 mg betamethasone is reached, dose reduction should be slower to allow the HPA-axis to recover.

Abrupt withdrawal of systemic corticosteroid treatment, which has continued up to 3 weeks is appropriate if it is considered that the disease is unlikely to relapse. Abrupt

withdrawal of doses of up to 6 mg daily of betamethasone, or equivalent for 3 weeks is unlikely to lead to clinically relevant HPA-axis suppression, in the majority of patients. In the following patient groups, gradual withdrawal of systemic corticosteroid therapy should be considered even after courses lasting 3 weeks or less:

- Patients who have had repeated courses of systemic corticosteroids, particularly if taken for greater than 3 weeks,
- When a short course has been prescribed within one year of cessation of long-term therapy (months or years),
- Patients who have reasons for adrenocortical insufficiency other than exogenous corticosteroids therapy,
- Patients receiving doses of systemic corticosteroid greater than 6 mg daily of betamethasone (or equivalent),
- Patients repeatedly taking doses in the evening.

During prolonged therapy any intercurrent illness, trauma or surgical procedure will require a temporary increase in dosage; if corticosteroids have been stopped following prolonged therapy, they may need to be temporarily reintroduced.

Special precautions

Particular care is required when considering the use of systemic corticosteroids in patients with the following conditions and frequent patient monitoring is necessary.

- Post-menopausal females as they are at particular risk of osteoporosis.
- Hypertension or congestive heart failure.
- Diabetes mellitus (or a family history of diabetes).
- History of tuberculosis.
- Glaucoma (or a family history of glaucoma).

- Previous corticosteroid-induced myopathy.
- Liver failure - blood levels of corticosteroid may be increased, (as with other medicines which are metabolised in the liver).
- Elderly persons.
- Renal insufficiency, chronic renal failure and uraemia.
- Epilepsy.
- Diverticulitis.
- Thromboembolic tendencies.

Psychiatric disturbances

Patients and /or carers should be warned that potentially severe psychiatric adverse reactions may occur with systemic steroids (see section 4.8). Symptoms typically emerge within a few days or weeks of starting treatment. Risks may be higher with high doses/systemic exposure, although dose levels do not allow prediction of the onset, type, severity or duration of reactions. Most reactions recover after either dose reduction or withdrawal, although specific treatment may be necessary.

Patients/carers should be encouraged to seek medical advice if worrying psychological symptoms develop, especially if depressed mood or suicidal ideation is suspected.

Patients/carers should also be alert to possible psychiatric disturbances that may occur either during or immediately after dose tapering/withdrawal of systemic steroids, although such reactions have been reported infrequently.

Particular care is required when considering the use of systemic corticosteroids in patients with existing or previous history of severe affective disorders in themselves or in their first degree relatives. These would include depressive or manic-depressive illness and previous steroid psychosis.

Pheochromocytoma Crisis

Pheochromocytoma crisis, which can be fatal, has been reported after administration of systemic corticosteroids, as in BETANOID TABLETS. Corticosteroids should only be administered to patients with suspected or identified pheochromocytoma after an appropriate risk/benefit evaluation.

Visual disturbance

Visual disturbance may be reported with systemic and topical corticosteroid use. If a patient presents with symptoms such as blurred vision or other visual disturbances, the patient should be considered for referral to an ophthalmologist for evaluation of possible causes which may include cataract, glaucoma or rare diseases such as central serous chorioretinopathy (CSCR) which have been reported after use of systemic and topical corticosteroids.

Elderly

The common adverse effects of systemic corticosteroids may be associated with more serious consequences in old age, especially osteoporosis, hypertension, hypokalaemia, diabetes, susceptibility to infection and thinning of the skin. Close clinical supervision is required to avoid life-threatening reactions.

Diabetic patients

The insulin requirements of diabetic patients are increased.

Sodium intake and potassium supplements

Sodium intake may need to be reduced and potassium supplements may be necessary.

Tumour lysis syndrome (TLS)

In post marketing experience tumour lysis syndrome (TLS) has been reported in patients with malignancies, including haematological malignancies and solid tumours, following the use of systemic corticosteroids alone, including BETANOID INJECTION 4mg/ml, or in combination with other chemotherapeutic medicines. Patients at high risk of TLS, such as patients with tumours that have a high proliferative rate, high tumour burden and high sensitivity to cytotoxic medicines, should be monitored closely and appropriate precautions should be taken.

Paediatric population

Caution is advised in children as they are more susceptible to systemic toxicity from betamethasone, as in BETANOID TABLETS**.**

Corticosteroids, as in BETANOID TABLETS, cause dose-related growth retardation in infancy, childhood and adolescence, which may be irreversible. Treatment should be limited to the minimum dosage for the shortest possible time. In order to minimize suppression of the HPA axis and growth retardation, consideration should be given to administration of a single dose on alternate days.

4.5 Interaction with other medicinal products and other forms of interaction

Steroids may reduce the effects of anticholinesterases in myasthenia gravis, cholecystographic X-ray media and non- steroidal anti-inflammatory medicines.

Hepatic enzyme inducers (e.g., aminoglutethemide, barbiturates, phenytoin, carbamazepine, primidone, rifabutin, rifampicin)

Concurrent administration of barbiturates (phenobarbitone), phenytoin, primidone,

aminoglutethimide, ephedrine or rifampicin may enhance the metabolism and reduce the therapeutic effects of corticosteroids.

Hypoglycaemic medicines, antihypertensives and diuretics

The desired effects of hypoglycaemic medicines (including insulin), antihypertensives and diuretics are antagonised by corticosteroids, the hypokalaemic effects of acetazolamide, loop diuretics, thiazides or furosemide are enhanced.

Coumarin anticoagulants

The efficacy of coumarin anticoagulants may be enhanced by concurrent corticosteroid therapy and close monitoring of the INR or prothrombin time is required to avoid spontaneous bleeding.

Salicylates

The renal clearance of salicylates is increased by corticosteroids, as in BETANOID TABLETS, and steroid withdrawal may result in salicylate intoxication.

Theophylline, carbenoxolone, amphotericin B

The risk of hypokalaemia is increased with theophylline, ulcer healing medicines such as carbenoxolone and antifungals such as amphotericin B.

Cardiac glycosides

Increased toxicity may result if hypokalaemia occurs in patients on cardiac glycosides.

Ritonavir and oral contraceptives

Ritonavir and oral contraceptives may result in increased plasma concentrations of corticosteroids, as in BETANOID TABLETS.

Mifepristone

The effect of corticosteroids, as in BETANOID TABLETS, may be reduced for 3-4 days after mifepristone.

Somatropin

The growth promoting effect of somatropin may be inhibited by corticosteroids as in BETANOID TABLETS.

Non-steroidal anti-inflammatory drugs (NSAIDs)

An increase in the incidence of gastrointestinal bleeding may occur if NSAIDS are taken concomitantly with corticosteroids, as in BETANOID TABLETS.

Vecuronium

Corticosteroids, as in BETANOID TABLETS, may antagonise the effects of neuromuscular blocking medicines such as vecuronium.

Fluoroquinolones

Concurrent use of corticosteroids, as in BETANOID TABLETS, and fluoroquinolones may result in increased risk of tendon rupture.

Quetiapine

Concomitant use of betamethasone, as in BETANOID TABLETS, with quetiapine may result in the increased metabolism of quetiapine and, depending on the clinical response, a higher dose of quetiapine may need to be considered.

CYP3A inhibitors

Co-treatment with CYP3A inhibitors, including cobicistat-containing products, is expected to increase the risk of systemic side-effects. The combination should be avoided unless the benefit outweighs the increased risk of systemic corticosteroid side effects, in which case patients should be monitored for systemic corticosteroid side effects.

Tretinoin

Corticosteroids may enhance the metabolism of tretinoin resulting in decreased levels of tretinoin.

4.6 Fertility, pregnancy and lactation

The safety and use of BETANOID TABLETS during pregnancy and in lactation has not been established.

Pregnancy

The ability of corticosteroids to cross the placenta varies between individual medicines, however, betamethasone, as in BETANOID TABLETS, readily crosses the placenta. Administration of corticosteroids to pregnant animals can cause abnormalities of foetal development including cleft palate, intra-uterine growth retardation and effects on brain growth and development.

There is no evidence that corticosteroids result in an increased incidence of congenital abnormalities, such as cleft palate/lip in man. However, when administered for prolonged periods or repeatedly during pregnancy, corticosteroids may increase the risk of intrauterine growth retardation.
Hypoadrenalism may, in theory, occur in the neonate following prenatal exposure to corticosteroids but usually resolves spontaneously following birth and is rarely clinically important. Myocardial hypertrophy and gastroesophageal reflux have been reported in association with in-utero exposure to betamethasone.

Betamethasone, as in BETANOID TABLETS, systemically administered to a woman during pregnancy may result in a transient suppression of the foetal heart rate parameters and biophysical activities that are widely used for the assessment of foetal well – being. These characteristics can include a reduction in foetal breathing movements, body movements and heart rate.

Breastfeeding

Corticosteroids may pass into breast milk, although no data are available for betamethasone, as in BETANOID TABLETS. Infants of mothers taking high doses of systemic corticosteroids for prolonged periods may have a degree of adrenal suppression

Fertility

There are no data in humans to evaluate the effect of corticosteroids on fertility.

4.7 Effects on ability to drive and use machines

BETANOID TABLETS has minor influence the ability to drive or operate machinery. Since adverse reactions such as blurred vision have been reported patients receiving, betamethasone, as in, BETANOID TABLETS, patients should not drive, use machinery or perform any tasks that require concentration, until they are certain that BETANOID TABLETS does not adversely affect their ability to do so.

4.8. Undesirable effects

a) Tabulated list of adverse reactions

System organ class	Frequent	Less frequent	Frequency unknown
Infections and infestations			Increased susceptibility and severity of infections with suppression of clinical symptoms and signs (masking of infections), opportunistic infections, recurrence of dormant tuberculosis.
Blood and the lymphatic system disorders			Leucocytosis.
Immune system disorders			Hypersensitivity including anaphylaxis has been reported.
Endocrine disorders			Cushings syndrome (moon face, buffalo hump, hirsutism, weight gain, flushing), suppression of the HPA axis, suppression of growth in infancy, childhood and adolescence, menstrual irregularity and amenorrhoea.
Metabolism and nutrition disorders			Hyperglycaemia with precipitation of the diabetic state, impaired carbohydrate tolerance with increased requirement for antidiabetic therapy*, retention of sodium and water with oedema excretion of potassium with the possibility of

			hypokalaemic alkalosis.
Psychiatric disorders	A wide range of psychiatric reactions**		
Nervous system disorders			Intracranial hypertension, neurological disturbances.
Eye disorders			Increased intra-ocular pressure, glaucoma, papilloedema, posterior subcapsular cataracts, corneal or scleral thinning, exacerbation of ophthalmic viral or fungal diseases, vision blurred (see also section 4.4).
Cardiac disorders			Myocardial rupture following recent myocardial infarction cardiac failure in extreme cases.
Vascular disorders			Thromboembolism hypertension, thrombo-embolic complications.
Gastrointestinal disorders			Abdominal distension, oesophageal ulceration, nausea, dyspepsia, peptic ulceration with perforation and haemorrhage acute pancreatitis, candidiasis gastric discomfort, hiccups, increased appetite.
Skin and subcutaneous tissue disorders			Impaired healing, skin atrophy, increased bruising, acne, telangiectasia, striae, Stevens-Johnson syndrome.
Musculoskeletal, connective tissue and bone disorders			Aseptic necrosis of bone, proximal myopathy, osteoporosis, vertebral and long bone fractures, avascular osteonecrosis, tendon rupture, spontaneous fractures.
General disorders and administrative site conditions			Hyperhidrosis, malaise.
Investigations			Nitrogen depletion.

* Negative protein, nitrogen and calcium balance. Increased appetite. Hyperhidrosis. Increased high - density lipoprotein and low – density lipoprotein concentrations in the blood. Fluid and electrolyte disturbance (Sodium and water retention, hypertension, potassium loss, hypokalaemic alkalosis).

** Including affective disorder (such as irritable, euphoric, depressed and labile mood and suicidal thoughts), psychotic reactions (including mania, delusions, hallucinations and aggravation of schizophrenia), behavioural disturbances, irritability, anxiety, sleep disturbances and cognitive dysfunction including confusion and amnesia have been reported. Reactions are common and may occur in both adults and children. In adults, the frequency of severe reactions has been estimated to the 5-6 %. Psychological effects have been reported on withdrawal of corticosteroids; the frequency is unknown. Psychological dependence.

b) Description of selected adverse reactions

Acute adrenal insufficiency during prolonged treatment, or on cessation of treatment. During long courses of corticosteroid therapy, patients should be seen regularly and checked for hypertension, glycosuria, hypokalaemia, gastric discomfort and mental changes.

Withdrawal symptoms and signs

Too rapid reduction of corticosteroid dosage following prolonged treatment can lead to acute adrenal insufficiency, hypotension and death (see section 4.4).

A 'withdrawal syndrome' may also occur including fever, myalgia, arthralgia, rhinitis, conjunctivitis, painful itchy skin nodules and loss of weight.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are requested to report any suspected adverse drug reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

Aspen Pharmacare:

E-mail: Drugsafety@aspenpharma.com

Tel: 0800 118 088 /+27 (0)11 239-6200

4.9 Overdose

Symptoms

Side effects can be precipitated and/or be of increased severity (see section 4.8).

Treatment

Treatment is symptomatic and supportive.

Treatment is unlikely to be needed in cases of acute overdosage.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and class: A 21.5.1 Corticosteroids and analogues

Pharmacotherapeutic group: Corticosteroids for systemic use, plain, Glucocorticoids,

ATC code: H02A B01

Betamethasone is a synthetic glucocorticoid analogue used for its anti-inflammatory effects.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Magnesium stearate, microcrystalline cellulose, povidone, sodium starch glycollate.

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

12 months

6.4. Special precautions for storage

Store at or below 25 °C.

Protect from light.

Keep the blisters in the carton until required for use.

6.5. Nature and contents of container

20 or 100 tablets are packed in a clear polyvinylchloride blister strip sealed with an aluminium foil backing. The blister strips are packed into an outer cardboard carton together with a leaflet.

Not all packs and pack sizes may be marketed.

6.6. Special precautions for disposal and other handling

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

PHARMACARE LIMITED

Healthcare Park

Woodlands Drive

Woodmead 2191

Hotline: 0800 122 912

8. REGISTRATION NUMBER

27/21.5.1/0543

9. DATE OF FIRST AUTHORISATION

30 September 1993

10. DATE OF REVISION OF TEXT

26 November 2024

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